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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/550,107	04/14/2000	Philippe Verwaerde	B0192/7013(ERP)	8463

7590 02/14/2002

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 02/14/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/550,107	Applicant(s) VERWAERDE ET AL.	
	Examiner Brian Whiteman	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-186* is/are pending in the application.

4a) Of the above claim(s) *2-7,14-16,21,22,31-35,45-50,63-73 and 88-90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8-13,17-20,23-30,36-44,51-62,74-87,91-97 and 101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 April 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *8* .

4a)98-100 and 102-186

DETAILED ACTION

Non Final Rejection

Priority

Receipt is acknowledged of papers (United Kingdom 9908670.4 filed on 4/15/1999) submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Priority to provisional 60/129,596 filed on 4/15/99 is acknowledged.

Information Disclosure Statement

The information disclosure statement filed on January 16, 2001 does not fully comply with the requirements of 37 CFR 1.98 because: applicant does not properly cite the journal article(s) listed on the 1449. The page numbers for journal articles (C22, C26 and C28) are incorrect.

References have been considered by the examiner, but in order to have the articles initialed and dated on the 1449, a new 1449 properly citing the journal articles must be filed with the response to this office action. Failure to comply with this notice will result in the above mentioned information disclosure statement being placed in the application file with the non-complying information not being considered. See 37 CFR 1.97(i).

Election/Restrictions

Response to election/restriction filed on 9/28/01 in paper no. 11 filed on 12/17/01 is acknowledged. Applicants elect Group I, claim 1, 2, 8-45, 51-99, 101, 105-126, 164, 165, and 179-186 and species restriction "biochemical, wild-type, adult worms, alpha-synuclein, SERCA and PLB proteins."

Applicants' traverse the species restriction for the following reasons: 1) The basis that the restriction to these individual species would not impose an undue burden on the Examiner, 2) The invention as claimed lies in the screening methodology and is largely independent of the genetic background of the nematode worms. See pages 1-2.

Applicants' traversal is acknowledged but is not found persuasive for the following reasons: the claims comprise of using several different and distinct worms (e.g. wild-type, humanized, mutant, or transgenic worms) in the distinct methods of the claimed invention. These products (worms) are classified under different classes and subclasses. In addition, the distinct worms require distinct steps to make each set of worms listed above. Furthermore, the assays for detecting a signal indicating phenotypic, physiological, behavioral, or biochemical changes in nematodes worms are distinct methods and require distinct steps to practice each distinct method. The worms listed above are distinct for the reasons given above and because the literature search required for wild type worms is not required for mutant, transgenic, or humanized worms, it would require an undue burden on the examiner to search each distinct group of worms. In addition, each distinct signal (e.g. phenotypic, physiological, behavioral, or biochemical) requires a distinct method with distinct steps to detect each signal. Thus, it would require an undue burden on the examiner to search each distinct signal and corresponding method.

In addition, claims 14-16, 45, and 88-90 read on the non-elected species (mutant, humanized, transgenic) and part of the non-elected invention because of the species elected encompassing wild-type worms.
Furthermore, claims 2, 21-22, 31-35, 45, 63-73, 98-99, 105-126, 164-165, and 179-186 are drawn to non-elected species. More specifically, claim 2 is drawn to a mutant strain of worms, claims 31-35 are directed to transgenic worms, and claims 98 and 105-126 are directed to detecting changes in movement behavior of the worms, which is not encompass in detecting

biochemical changes in worms. Thus, claims 2, 21-22, 31-35, 45, 63-73, 98-99, 105-126, 164-165, and 179-186 are considered part of the non-elected embodiment.

Thus, the restriction requirement is proper and is made final.

DV 2/11/02 Claims 2, 4-7, 14-16, 21-22, 31-35, 45-50, 63-73, 88-90, 98-100, and 102-186 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11.

Claim Objections

Claims 11-13, 18-20, 37, 53-56, 59-61, 78, 82, and 92- 94 are objected to because of the following informalities: Claim 53 is grammatically incorrect because of the phrase "detecting the said signal." Suggest removing either "the" or "said". Claims 11-13, 18-20, 37, 53-56, 59, 61, 78, 82, 92, and 92 should have a comma before the conjunction "and" and "or". Claims 19, 60, and 93 should state, "fluorescence activated nematode screening and sorting" before the abbreviation FANS. Appropriate correction is requested.

Claims 1, 8-13, 17-20, 23-30, 36-44, 51-62, 74-87, 91-97, and 101 are pending examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 8-13, 17-30, 36-44, 51-62, 74-87, 91-97, and 101 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 101 recites the limitation "behaviour part in (e)" in line 6, page 82. There is insufficient antecedent basis for this limitation in the claim. The claims (44, 81, and 82), which claim 101 depends on do not have a step (e). Clarification is requested.

The statement in claims 8-13, 17-30, 36-43, 51-62, 74-85, 87, 91-97, and 101, "**A** method as claimed in claim ..." is indefinite because it does not point out which method **a** method is referring to in the claims. The dependent claims should state "**The** method as claimed in claim...'

The term "means" in claim 1, 17, 19, 44, 53, 58, 60, 86, 91, and 93 is a relative term, which renders the claim indefinite. The term "means" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The disclosure does not define the metes and bounds of the term. Suggest changing the term to "device".

Claims 36, 40, 77, 81 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationship is: in the step of the method of identifying, where is the liquid assay medium located. Suggest rewording the claims to read "A method as claimed in claim .., wherein step (a) is performed in a multi well plate with liquid assay medium containing a water-soluble polymer at a concentration sufficient to increase viscosity of the medium".

Claims 38, 41, 43, 79, 82 and 84 are free of the prior art.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 8-11, 17-18, 23-30, 36-37, and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Rand et al. (Methods in Cell Biology, Vol. 48, 1995, IDS). Rand teaches combining compounds and C. elegans (wild type) in a method for studying the interaction of the two (pages 188, 191, and 200). Rand further teaches that micro-titer plates or other multi-well plates are useful for experiments because they permit many strains and/or drug concentrations to be tested in parallel (pages 191, 193, 200). In addition, Rand teaches that the experiment can take place in liquid medium or on agar plates (pages 190-191). It would be anticipated, absence evidence to the contrary, that when the worms are placed in a liquid medium, they would not stick to the plate. Furthermore, Rand teaches that it is important to use synchronous populations to determine state-specific effects directly (page 191). Rand further discusses using a quantitative assay for resistance/sensitivity to the drug being tested; absence evidence to the contrary, could be a plate reader, which is a standard piece of laboratory equipment that is used to perform quantitative assays involving a multi-well plate.

Claims 1, 8, 9, 23-30, 36-37, 40, 42, 44, 51-52, 74-78, 81, 83, and 85 are rejected under 35 U.S.C. 102(b) as being anticipated by Avery (IDS, The Journal of Experimental Zoology, Vol. 252, pp. 263-270, pp 1990). Avery teaches an assay that allows measurement of the pharynx-pumping rate in a population of worms suspended in a liquid medium by measuring their uptake of iron particles (abstract). In addition, the assay is also useful for measuring effects of drugs on pumping (abstract). Avery further teaches that using wild-type worms (including some hermaphrodites) for pumping assay were grown on plates with 3% agar (pages 264 and 265). Furthermore, absence evidence to the contrary, using a multi well plate, adding an equal number of worms into each well of a plate, and using worms that are synchronizes in the same growth stage is routine practice in the art of using worms to study properties of a chemical interaction.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 8-11, 17-18, 23-30, 36-37, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rand (Methods in Cell Biology, Vol. 48, 1995, IDS), taken with Leitch et al. (IDS, Antimicrobial Agents and Chemotherapy, Vol. 41, 1997, pp. 337-344). Rand teaches combining compounds and C. elegans [wild types] (pages 188 and 200). Rand teaches combining compounds and C. elegans in a method of studying the interaction of the two (pages 188, 191, and 200). Rand further teaches that micro-titer plates or other multi-well plates are useful for experiments because they permit many strains and/or drug concentrations to be tested in parallel (pages 191, 193, 200). In addition, Rand teaches that the experiment can take place in liquid medium or on agar plates (pages 190-191). It would be obvious to one of ordinary skill in the art, absence evidence to the contrary, that when the worms are placed in a liquid medium, they would not stick to the plate. Furthermore, Rand teaches that it is important to use synchronous populations to determine state-specific effects directly (page 191). Rand further discusses using a quantitative assay for resistance/sensitivity to the drug being tested; absence evidence to the contrary, could be a plate reader, which is a standard piece of laboratory equipment that is used to perform quantitative assays involving a multi-well plate. However,

Rand does not teach a method of identifying a chemical substance, which has potential pharmacological activity using nematodes worms, which method comprises the step of detecting a signal comprises detecting a change in a measurable property of a marker molecule, wherein the marker molecule is a fluorescent molecule.

However, at the time the invention was made, a method using a test system with a fluorescent probe to assess the activity of a substance using confocal microscopy to visualize the fluorescent probe calcein within infected cells of a parasite was well known in the art (Leitch, page 337). Using this method, the viability of the parasite can be studied.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made as routine practice to combine the teaching of Rand taken with Leitch, namely to used a fluorescent probe in a method of identifying a chemical substance, which has potential pharmacological activity using nematodes worms, which method comprises the step of detecting a signal comprises detecting a change in a measurable property of a marker molecule. One of ordinary skill in the art would have been motivated to combine the teaching because to study the activity of a chemical substance after contacting the worms with the substance one skilled in the art would need a probe (e.g. fluorescent). Furthermore, the substance can be studied in living worms, without having to kill the worms and to isolate the desired cells for *in vitro* studying.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1, 8-11, 17-18, 23-30, 36-37, 44, 86, 87, 91-92, and 95-97 are rejected under 35 U.S.C. 102(a) as being unpatentable over Kerr et al. (West Coast Worm Meeting, abstract 77,

1998, http:/elegans.swmed.edu/WCWM/98/) taken with Rand (Methods in Cell Biology, Vol. 48, 1995, IDS). Kerr teaches imaging calcium transients in a subset of excitable cells in C. elegans. Kerr used the myo-2 promoter to express cameleon in the pharyngeal muscle of C. elegans and study the expression with an imaged two-photon confocal microscopy. However, Kerr does not specifically teach a method of identifying a chemical substance, which has potential pharmacological activity using nematodes worms placed in equal number in multi-well plates, which method comprises the step of detecting a signal indicating a biochemical change using non-visual detection device, multi well plates and a liquid medium or agar medium.

However, at the time the invention was made, Rand teaches combining compounds and C. elegans (wild type) in a method of studying the interaction of the two (pages 188, 191, and 200). Rand further teaches that micro-titer plates or other multi-well plates are useful for experiments because they permit many strains and/or drug concentrations to be tested in parallel (pages 191, 193, 200). In addition, Rand teaches that the experiment can take place in liquid medium or on agar plates (pages 190-191). It would be obvious to one skilled in the art, absence evidence to the contrary, that when the worms are placed in a liquid medium, they would not stick to the plate. Furthermore, Rand teaches that it is important to use synchronous populations to determine state-specific effects directly (page 191). Rand further discusses using a quantitative assay for resistance/sensitivity to the drug being tested, which absence evidence to the contrary, one of ordinary skill in the art would used a plate reader, which is a standard piece of laboratory equipment that is used to perform quantitative assays involving a multi-well plate.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made as routine practice to combine the teaching of Kerr taken with Rand,

namely to used a marker in a method of identifying a chemical substance, which has potential pharmacological activity using nematodes worms, which method comprises the step of detecting a signal comprises detecting a change in a measurable property of a marker molecule. One of ordinary skill in the art would have been motivated to combine the teaching because it was routine in the art as taught by Rand to use multi-well plates, a multi-well plate reader, and liquid medium or agar plates for studying compound interactions in worms.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1, 8-11, 17-20, 23-30, 36-37, and 39-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rand (Methods in Cell Biology, Vol. 48, 1995, IDS) taken with Miwa et al. (US Patent No. 4,444,981, IDS) in further view of applicants' own admission that a non-visual detection system is commercially available from UNION BIOMETRICA, INC (page 7, lines 14-26 of the specification). Rand teaches combining compounds and C. elegans (wild type) in a method of studying the interaction of the two (pages 188, 191, and 200). Rand further teaches that micro-titer plates or other multi-well plates are useful for experiments because they permit many strains and/or drug concentrations to be tested in parallel (pages 191, 193, 200). In addition, Rand teaches that the experiment can take place in liquid medium or on agar plates (pages 190-191). It would have been obvious to one skilled in the art, absence evidence to the contrary, that when the worms are placed in a liquid medium, they would not stick to the plate. Furthermore, Rand teaches that it is important to use synchronous populations to determine state-specific effects directly (page 191). Rand further discusses using a quantitative assay for resistance/sensitivity to the drug being tested, which absence evidence to the contrary could be a

plate reader, which is a standard piece of laboratory equipment that is used to perform quantitative assays involving a multi-well plate. However, Rand does not teach a method of identifying a chemical substance, which has potential pharmacological activity using nematodes worms, which method comprises the step of detecting a signal comprises detecting a biochemical changes in the nematode worms using non-visual detection means, wherein the non-visual detection means is a FANS device.

However, at the time the invention was made, Miwa teaches that the chemical industry is producing novel chemical substances and research is being done to find new applications for known chemical substances (column 1, line 40-45). In each case, it is desirable to establish a rapid method for testing substances (column 1, lines 45-47).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Rand taken with Miwa in further view of applicants' own admission, namely to produce a method of identifying a chemical substance, which has potential pharmacological activity using nematodes worms, which method comprises the step of detecting a biochemical signal using a high throughput screening system. One of ordinary skill in the art would have been motivated to combine the teaching because the device offers high throughput screening.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1, 36-37, and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rand (Methods in Cell Biology, Vol. 48, 1995, IDS) taken with Balan (Applicants' IDS, Journal of Chemical Ecology, Vol. 11, 1985, pp. 105-111). Rand teaches combining compounds and C.

elegans (wild type) (pages 188 and 200). Rand further teaches that micro-titer plates are useful for experiments; they permit many strains and/or drug concentrations to be tested in parallel (pages 191 and 193). In addition, Rand teaches that the experiment can take place in liquid medium or on agar plates and also teaches what the age of the worms should be (pages 190-191). However, Rand does not teach a method of identifying a chemical substance, which has potential pharmacological activity using nematodes worms, which method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to increase the viscosity of the medium, wherein the concentration of water soluble polymer in the liquid medium is 0.3%.

However, at the time the invention was made, Balan teaches a simple method for the experimental determination of minimal concentrations of attractants by the nematode *Panagrellus redivivus* (abstract). Balan teaches using a 0.3% agar plate with the attractant and two similar control disks not containing the attractant (Figure 1, page 106). Balan further teaches that this method could also be used with other nematodes and/or for the research of nematode repellant substances (page 111).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Rand taken with Balan, namely to produce a method of identifying a chemical substance, which has potential pharmacological activity using nematodes worms, which method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to increase the viscosity of the medium. One of ordinary skill in the art would have been motivated to combine the teaching because the assay is

simple and would save one skilled in the art time in assaying potential pharmacological substances.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1, 23-30, 36-37, 39, 40, 42, 44, 51-54, 58-62, 74-78, 80, and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Avery (IDS, The Journal of Experimental Zoology, Vol. 252, pp. 263-270, pp 1990) taken with Miwa et al. (US Patent No 4,444,981, IDS) in further view of applicants' own admission that a non-visual detection system is commercially available from UNION BIOMETRICA, INC (page 7, lines 14-26 of the specification). Avery teaches an assay that allows measurement of pumping rate in a population of worms suspended in liquid by measuring their uptake of iron particles (abstract). In addition, the assay is also useful for measuring effects of drugs on pumping (abstract). Avery further teaches that using wild-type worms for pumping assay were grown on plates with 3% agar (page 264) and using hermaphrodite worms in the assays (pages 264 and 265). However, Avery does not teach a method of identifying a chemical substance, which has potential pharmacological activity using nematodes worms, which method comprises the step of detecting a signal comprises detecting a biochemical changes in the nematode worms using non-visual detection means, wherein the non-visual detection means is a FANS device.

However, at the time the invention was made, Miwa teaches that the chemical industry is producing novel chemical substances and research is being done to find new applications for known chemical substances (column 1, line 40-45). In each case, it is desirable to establish a rapid method for testing substances (column 1, lines 45-47).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made as routine practice to combine the teaching of Avery taken with Miwa in further view of applicants' own admission that a non-visual detection system is commercially available from UNION BIOMETRICA, INC (page 7, lines 14-26 of the specification), namely to produce a method of identifying a chemical substance, which has potential pharmacological activity using nematodes worms, which method comprises the step of detecting a biochemical signal with a high throughput device. One of ordinary skill in the art would have been motivated to combine the teaching because the device offers high throughput screening.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1, 8-11, 17-20,23-30, 36, 37, 39, 44, 53-61, 85-87, and 91-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Kerr et al. (West Coast Worm Meeting, abstract 77, 1998, http:/elegans.swmed.edu/WCWM/98/) taken with Miwa et al. (US Patent No 4,444,981, IDS) in further view of applicants' own admission that a non-visual detection system is commercially available from UNION BIOMETRICA, INC (page 7, lines 14-26 of the specification). Kerr teaches imaging calcium transients in a subset of excitable cells in C. elegans. Kerr used the myo-2 promoter to express cameleon in the pharyngeal muscle of C. elegans and imaged two-photon confocal microscopy. However, Kerr does not teach a method of identifying a chemical substance, which has potential pharmacological activity using nematodes worms, which method comprises the step of detecting a signal comprises detecting a biochemical changes in the nematode worms using non-visual detection means, wherein the non-visual detection means is a FANS device.

However, at the time the invention was made, Miwa teaches that the chemical industry is producing novel chemical substances and research is being done to find new applications for known chemical substances (column 1, line 40-45). In each case, it is desirable to establish a rapid method for testing substances (column 1, lines 45-47).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made as routine practice to combine the teaching of Kerr taken with Miwa in further view of applicants' own admission, namely to produce a method of identifying a chemical substance, which has potential pharmacological activity using nematodes worms, which method comprises the step of detecting a biochemical signal with a high throughput screening device. One of ordinary skill in the art would have been motivated to combine the teaching because the device offers high throughput screening.

Claims 1, 8, 9, 10, 11, 44, 86, 87, and 91-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kerr et al. (West Coast Worm Meeting, abstract 77, 1998, http:/elegans.swmed.edu/WCWM/98/) taken with Miwa et al. (US Patent No 4,444,981, IDS) in further view of applicants' own admission that a non-visual detection system is commercially available from UNION BIOMETRICA, INC (page 7, lines 14-26 of the specification). Kerr teaches imaging calcium transients in a subset of excitable cells in C. elegans. Kerr used the myo-2 promoter to express cameleon in the pharyngeal muscle of C. elegans and imaged two-photon confocal microscopy. However, Kerr does not teach a method of identifying a chemical substance, which has potential pharmacological activity using nematodes worms, which method comprises the step of detecting a signal comprises detecting a biochemical changes in the

nematode worms using non-visual detection means, wherein the non-visual detection means is a FANS device.

However, at the time the invention was made, Miwa teaches that the chemical industry is producing novel chemical substances and research is being done to find new applications for known chemical substances (column 1, line 40-45). In each case, it is desirable to establish a rapid method for testing substances (column 1, lines 45-47).

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Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1, 44, 51-59, 74-78, 80, and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Avery taken with Miwa and applicants' own admission that a non-visual detection system is commercially available from UNION BIOMETRICA, INC (page 7, lines 14-26 of the specification) taken with any Mysore et al. (Mol. Plan. Microbe Interact., 1998, Vol. 11 abstract), Obexer et al. (Trop. Med. Parasitol. Vol. 46 1995, abstract), Denham et al. (Cytometry,

Vol. 19, 1996, abstract), Huan et al. (J. Immunol. Methods, Vol. 149, 1992, abstract), Yang et al. (Cell Transplant, Vol. 7, 1998, abstract), and Stevens et al., (Mol. Cell. Probes, 1996, Vol. 10, abstract).

The rejection of the base claims 1, 44, 51-55, 74-78, 80, 85 under 35 U.S.C. 103(a) is applied here as indicated above, by Avery taken with Miwa in further view of applicants' admission that a non-visual detection system is commercially available from UNION BIOMETRICA, INC (page 7, lines 14-26 of the specification). However, Avery taken with Miwa in further view of in further view of applicants' own admission do not specifically teach the specific markers consisting of a calcein-AM, BCECF-AM, FDP, FDA, AMPPD, or X-gluc.

However, at the time the invention was made, the fluorescent, luminescent, or a coloured markers listed above were well known in the art, flourescein diphosphate (FDP) (Huang), fluorescein diacetate (FDA) (Yang), X-gluc (Mysore), BCECF-AM (Obexer), AMPPD (Stevens), or calcein-AM (Denholm) for labeling cells.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made as routine practice to interchangeable use any marker taught by Huang, Yang, Mysore, Obexer, Stevens, or Denholm in a method taught by the teaching of Avery taken with Miza and in further view of applicants' own admission that a non-visual detection system is commercially available from UNION BIOMETRICA, INC (page 7, lines 14-26 of the specification), namely to produce a method of identifying a chemical substance, which has potential pharmacological activity using nematodes worms, which method comprises the step of detecting a signal comprises detecting a change in a measurable property of a marker molecule, wherein the marker molecule is a flourescein diphosphate (Huang), fluorescein diacetate (Yang),

AMPPD, X-gluc (Mysore), BCECF-AM (Obexer), AMPPD (Stevens), and calcein-AM (Denholm). One of ordinary skill in the art would have been motivated to use any of the markers because of the routine applications of using any of these markers for labeling cells.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ms. Tracey Johnson whose telephone number is (703) 305-2982. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, primary examiner, Dave Nguyen can be reached at (703) 305-2024.

If attempts to reach the primary examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-2742.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635
February 11, 2001

DAVE T. NGUYEN
PRIMARY EXAMINER